A1 Cont

showing a decrease of 25% or more in M proteins (Blood, 90, 3743-3750, 1997). Therefore, it becomes more and more necessary to establish a novel therapy for bone lesions accompanying multiple myeloma from the viewpoint of patients' QOL.

Pages 4-5, please replace the first full paragraph with the following:

A2

Recently, studies have been made on the anticancer effects of BP's and it is reported that several BP's have an effect of inhibiting cell proliferation *in vitro* (Britishi J. Haematology, 98, 665-672, 1997), though any clinical usefulness has been proved in none of these cases and some reports rather denying the anticancer effect of BPs are also presented. That is to say, it is reported that pamidronate has been used in a murine model of myeloma, and although no effect on tumor growth was demonstrated, there was evidence of a cytotoxic effect within the bone marrow. It is also reported that risedronate has been used in a murine model of myeloma; however, although there was a clear reduction in bone destruction, no effect on tumor burden was noted (Leukemia and Lymphoma, 32, 129-138, 1998). In a patient who was intravenously administered in a higher dose than in prior clinical studies, a transient decrease in a cancer marker was observed. However, it is reported that it is possible that for a cytostatic or even cytotoxic effect to occur, higher dose or more frequent administration of pamidronate is required compared to dosing for its beneficial bone effects (Britishi J. Haematology, 103, 530-532, 1998). Accordingly, it has never been reported hitherto that BPs exert an anticancer effect (i.e., a therapeutic effect on multiple myeloma) in patients with multiple myeloma.

Page 14, please replace the first and second full paragraphs with the following:

A3

In case of usual oral administration, the daily dose ranges from about 1 to 20 mg, preferably from about 3 to 10 mg and still preferably from about 6 to 9 mg. The daily dose is

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administered once a day or divided into 2 to 4 doses per day. The dose may be appropriately determined case by case taking the body weight, conditions, age, sex, etc. of the patient into consideration.

In case of intravenous administration, the single dose ranges from about 0.1 to 10 mg, preferably from about 0.1 to 5 mg and still preferably from about 0.5 to 2 mg. The composition can be intravenously dripped in this dose once in 2 to 6 weeks, preferably once in 3 to 5 weeks and still preferably once in 4 weeks over 10 to 60 minutes (preferably 30 minutes). The dose may be appropriately determined case by case taking the body weight, conditions, age, sex, etc. of the patient into consideration.

Page 15, please replace the first full paragraph with the following:

A4

Fig. 1 is a diagram which shows the bone resorption inhibition level with the use of urinary deoxypyridinoline level as a marker. Each column in this figure represents mean ± standard error. Number of mice is indicated in columns. Comparisons with the sham-operated group and the solvent group with paralysis in hind limb were performed with the Student's t-test. * significantly different from the solvent group with paralysis in hind limb. (**: Dunnett's multiple range test, $p<0.01$).

Page 15, please replace the third full paragraph with the following:

A5

Fig. 3 shows changes in urinary Dpyr level (a bone resorption marker) in 4 weeks after the oral administration of the compound A (6 mg/day) in Example 5. In this figure, the abscissa indicates time (weeks) after the start of the administration, while the ordinate indicates the Dpyr level referring the Dpyr level before the administration as to 100%. The pamidronate data in this